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UNITED STATES ARMY
BIOLOGICAL CENTER
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Physical Defense Division
COMMODITY DEVELOPMENT AND ENGINEERING LABORATORY

Project 1C622401A071

April 1966

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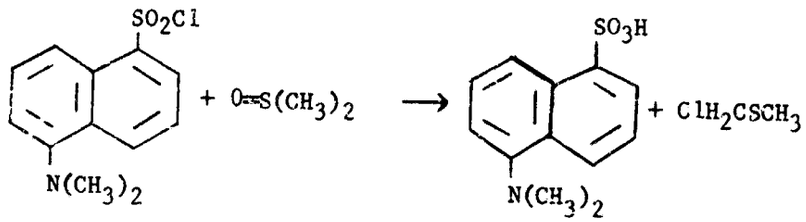
ABSTRACT

The reaction of dimethylsulfoxide and 5-dimethylaminonaphthalene-1-sulfonyl chloride was studied under the conditions of a pseudo-unimolecular reaction with the dimethylsulfoxide in excess. The reaction produced 5-dimethylaminonaphthalene-1-sulfonic acid and chlorodimethyl sulfide. The mean rate of disappearance of the sulfonyl chloride was measured as $1.123 \pm 0.232 \times 10^{-3}$ sec^{-1} and the appearance of the sulfonic acid as $1.404 \pm 0.229 \times 10^{-3}$ sec^{-1} based upon the initial concentration of the sulfonyl chloride. Chlorodimethyl sulfide was identified by gas chromatography and the sulfonic acid by its absorption properties and decomposition point. A reaction mechanism is proposed based on a sulfoxonium intermediate.

I. INTRODUCTION

Dimethylsulfoxide (DMSO) has been used extensively in recent years because of its unique solvent and reaction characteristics.[1,2] In the course of testing DMSO as a solvent and stabilizer for 5-dimethylamino-naphthalene-1-sulfonyl chloride (DANSC) in protein staining, we have observed a rapid reaction at room temperature that resulted in a change in the absorption characteristics and produced a fluorescence emission. This paper presents a simple kinetic analysis of the reaction and a proposed mechanism for the formation of 5-dimethylaminonaphthalene-1-sulfonic acid (DANSA) and chlorodimethyl sulfide (CDMS) via a sulfoxonium salt intermediate that can be formulated empirically as:

DANSC + DMSO → DANSA + CDMS



II. EXPERIMENTAL

A. MATERIALS

DANSC, DANSA, and CDMS were obtained from the K and K Labs, Inc., New York, and the DMSO and ether were reagent grade from Fisher Scientific Co., Silver Spring, Maryland. The materials were used without further purification. The molar absorptivities were determined as follows:

DANSC in ether, $\epsilon_{360m\mu} = 3.62 \times 10^3$, DANSA in DMSO, $\epsilon_{322m\mu} = 4.77 \times 10^3$

In a mixture of DMSO and ether the wavelength of maximum absorbance for DANSA shifted to 316 mμ but ε remained the same.

B. KINETICS

The decrease in absorbance at 360 mμ for DANSC and increase at 316 mμ for DANSA were followed simultaneously on a Beckman DK-2 spectrophotometer equipped with an automatic repetitive scanning attachment using 1.0-cm quartz cuvettes. The spectrum was scanned from 365 mμ to 265 mμ with a scanning time of approximately 90 seconds. The reaction was followed for approximately 20 minutes; the exact times were recorded for each experiment. The order of addition of reagents was always the same. Starting with a given volume and concentration of DANSC in ether, ether and DMSO were added in the proportions required to give the final desired concentrations. All reaction times were measured from the time of addition of the DMSO. The DANSC concentration ranged from 0.61×10^{-4} to 1.85×10^{-4} M. The DMSO concentration was 6.15 M to give a large excess consistent with a pseudo-unimolecular reaction. All of the kinetic studies were made at room temperature. Ether was chosen as a reaction solvent to prevent complicated side reactions.[3]

C. IDENTIFICATION OF REACTION PRODUCTS

The increase in the absorbance at 316 mμ served to identify the DANSA formed in the reaction. It was further identified in a preparative experiment described later. The CDMS was identified by gas chromatography using a 4 ft x 6 mm column of Carbowax-20 M (5%), Haloport F (30/60 mesh) with programming at 11 C per min from 60 to 170 C on an F and M model 500 gas chromatograph. The CDMS identification was confirmed by comparison of the peak and retention time with an authentic sample.

In a preparative experiment, the reaction mixture was allowed to stand for 24 hours at room temperature. A sample was removed and gas-chromatographed as before. Only two peaks were observed and these were confirmed to be DMSO and CDMS with authentic samples treated the same way. The ether was removed from the remaining reaction mixture by gentle heating on a water bath and 1.0 ml of the residual solution was removed, diluted to 100 ml with DMSO, and examined spectrophotometrically. A single peak was observed at 322 mμ as evidence of the presence of DANSA. The remaining solution was treated according to the procedure of Laurence.[4] A solid material was obtained which when recrystallized from 0.1 HCl had a decomposition point of 292 C (uncorrected) compared with 294 C (uncorrected) for an authentic sample. Quantitative recovery of the DANSA was not made because of its extreme solubility in DMSO. The isolated material redissolved in DMSO showed only one absorbance peak at 322 mμ, substantiating the presence of DANSA.

III. RESULTS

Figure 1 is a reproduction of a repetitive scan spectrum for a single kinetic experiment. From this set of curves and others the absorbance at 360 mμ and 316 mμ was determined and plotted as a function of time and the slopes were determined. The logarithms of these slopes were plotted against the logarithms of the concentration of DANSC to establish the order of the reaction as a function of the concentration of DANSC. Figure 2 shows the results for the appearance of DANSA and the disappearance of DANSC. Both slopes are approximately one, indicating first-order dependence. Further first-order dependence was confirmed using the integrated rate equations, half-life dependence, and by the differential method. The first-order rate constant for the disappearance of DANSC was $1.123 \pm 0.232 \times 10^{-3}$ sec^{-1} and for the appearance of DANSA was $1.404 \pm 0.229 \times 10^{-3}$ sec^{-1} as a function of the initial concentration of the DANSC.

When the concentration of DMSO was varied over approximately a three-fold range at constant concentration of DANSC, a linear dependence on DMSO concentration was observed. According to Taylor,[6] under the conditions of a pseudo-unimolecular reaction these rates are only apparent. Dividing each of these rates by the corresponding concentration of the DMSO initially present gives the true rate as $1.55 \pm 0.270 \times 10^{-4}$ sec^{-1}.

IV. DISCUSSION

The adherence of the results of the reaction to the pseudo-unimolecular kinetics as a function of the concentration of DANSC and the constancy of the rate as a function of the DMSO are indicative of a bimolecular reaction. The presence of a isosbestic point in Figure 1 at 340 mμ, although not absolute proof, indicates only two reactants; the identification of only two products of the reaction is additional evidence for the formulation of the reaction as shown in the equation on page 5. Further, Bordwell and Pitt[6] have shown CDMS and benzoic acid and CDMS and HCl to be products of the reaction of DMSO with benzoyl and thionyl chloride respectively. With silicon tetrachloride, Lappert[9] has shown the products to be CDMS and HCl. DMSO has also been shown to react with a variety of materials such as aromatic sulfonic acid esters,[7] sulfonamides,[8] alcohols,[9] and phenols.[10,11]

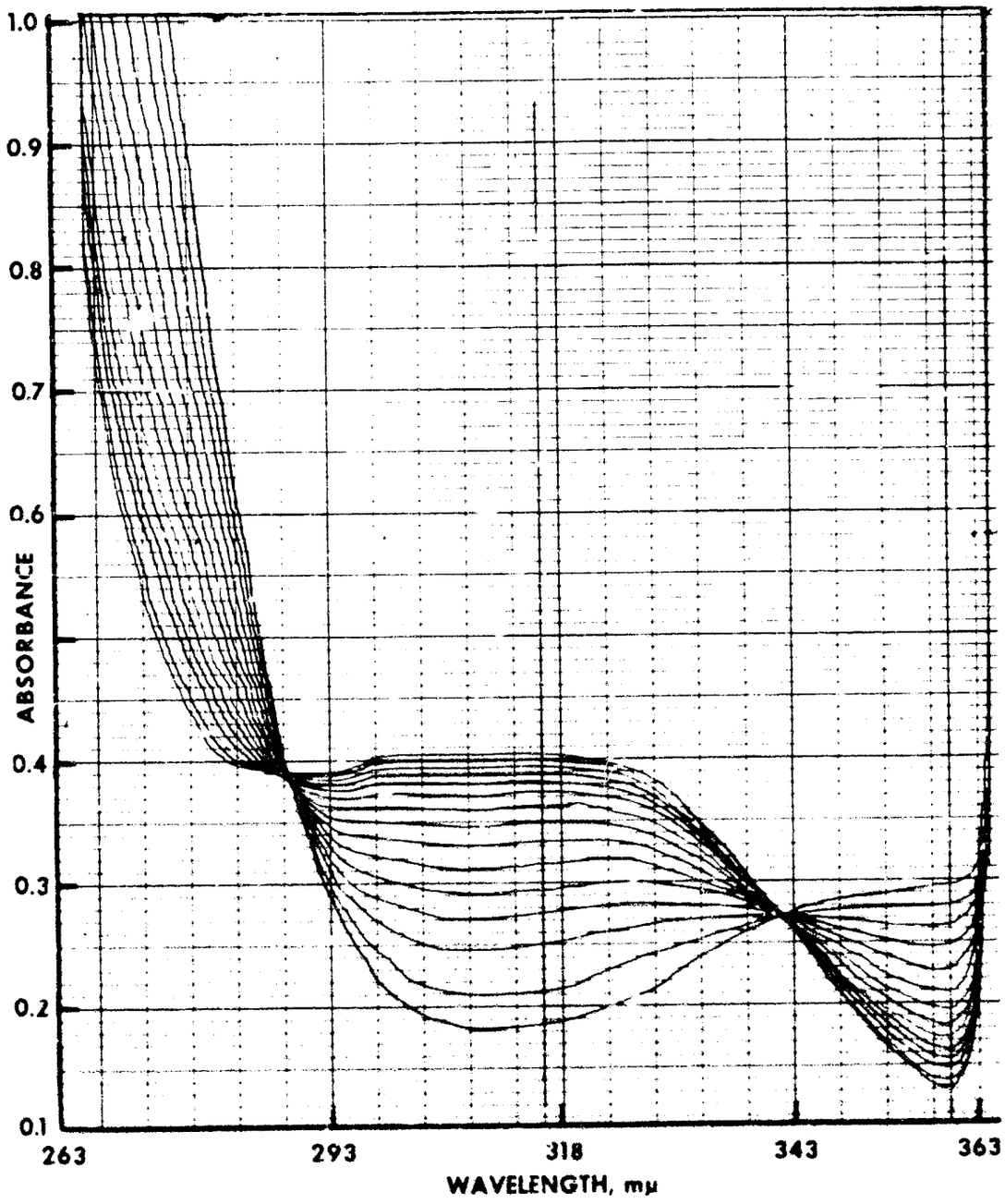


Figure 1. Repetitive Scan Spectra. Concentration of DANSC = 0.92 x 10^{-4} M, DMSO = 6.15 M. Solvent, ethyl ether.

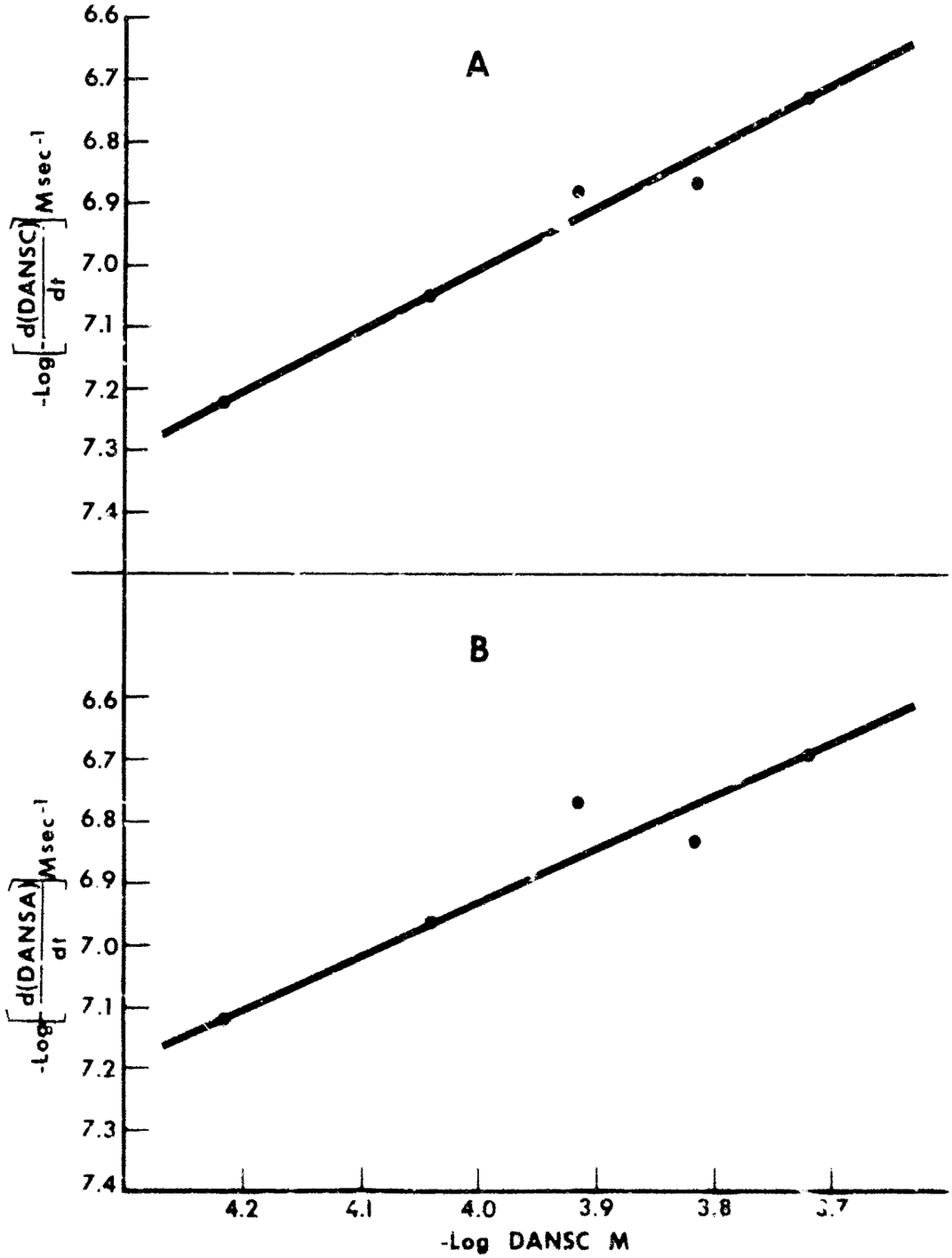
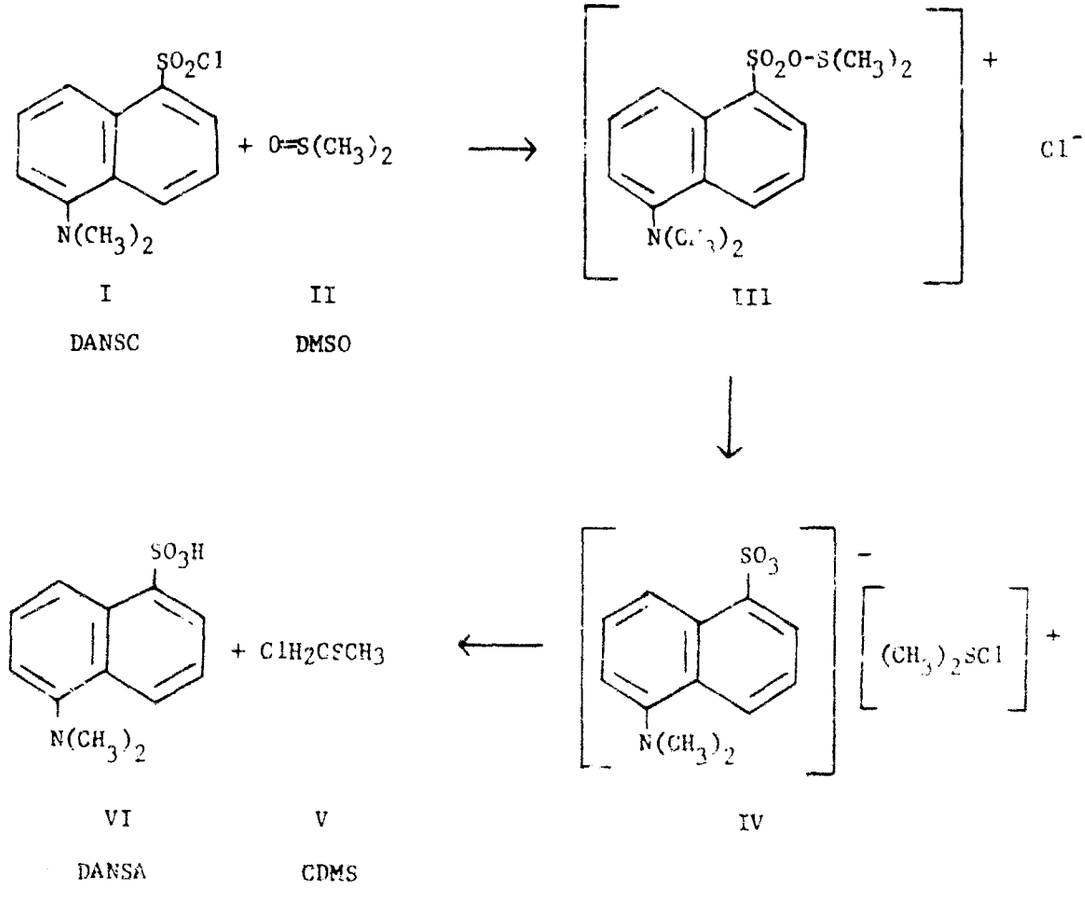


Figure 2. Reaction Rates. (A) Logarithm of the rate of disappearance of DANSC as a function of the logarithm of the initial concentration of DANSC. (b) Logarithm of the rate of appearance of DANSA as a function of the logarithm of the initial concentration of DANSC.

A suggested mechanism for the reaction is given in the following scheme, beginning with a nucleophillic attack by the DMSO (II) on the sulfur containing the chloride in DANSC (I) with the formation of a sulfoxonium intermediate (III). The chloride ion then displaces the oxygen-containing group in (III) by attack at the sulfur ion to give the sulfonium compound (IV), which rearranges to give CDMS (V) and DANSA (VI).



This proposed mechanism is consistent with that proposed for the reaction of the [illegible]th organic and inorganic acyl halides,[6,7] anhydrides,[10,13] and alkyl [illegible]des.[14]

Although the reaction in ether at room temperature proceeded moderately gas chromatographic and spectrophotometric analyses of the reaction mixture gave no indication of other products, it was noted that wh the DANSC was added directly to DMSO the solution became warm and passed through several color changes from red to yellow to colorless. This change in color was not investigated but it might possibly be related to the intermediates formed.

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